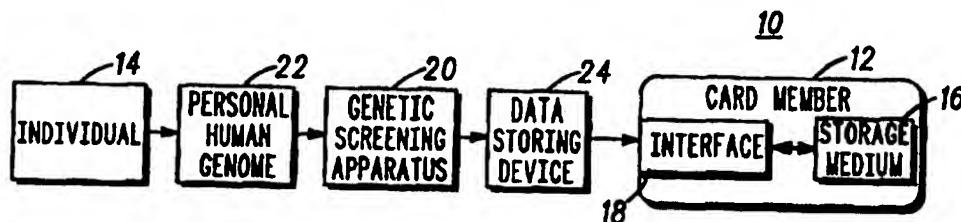




## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

|   |           |   |
|---|-----------|---|
| (51) International Patent Classification <sup>6</sup> :<br><b>G06K 7/08</b>   | <b>A1</b> | (11) International Publication Number: <b>WO 97/31327</b><br>(43) International Publication Date: <b>28 August 1997 (28.08.97)</b>  |
| <p>(21) International Application Number: <b>PCT/US96/19690</b></p> <p>(22) International Filing Date: <b>11 December 1996 (11.12.96)</b></p> <p>(30) Priority Data:<br/><b>08/606,985</b>      <b>26 February 1996 (26.02.96)</b>      <b>US</b></p> <p>(71) Applicant (for all designated States except US): <b>MOTOROLA INC. [US/US]; 1303 East Algonquin Road, Schaumburg, IL 60196 (US).</b></p> <p>(72) Inventors; and<br/>(75) Inventors/Applicants (for US only): <b>REBER, William, L. [US/US]; 1029 Bucaneer Road #6, Schaumburg, IL 60916 (US). PERTTUNEN, Cary, D. [US/US]; 11764 Raintree Court, Shelby Township, MI 48315 (US).</b></p> <p>(74) Agents: <b>SARLI, Anthony, J., Jr. et al.; Motorola Inc., Intellectual Property Dept., 1303 East Algonquin Road, Schaumburg, IL 60196 (US).</b></p> |           | <p>(81) Designated States: <b>AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</b></p> <p><b>Published</b><br/><i>With international search report.</i></p> |

(54) Title: **PERSONAL HUMAN GENOME CARD AND METHODS AND SYSTEMS FOR PRODUCING SAME**

## (57) Abstract

A personal genome card (10) includes a card member (12) and a machine-readable storage medium (16) integrated in the card member. Machine-readable data including a representation of a sequence of nucleotide bases for at least a portion of a genome of an individual (22) is stored on the machine-readable storage medium (16). The machine-readable data can further include phenotype information for the individual, a personal medical history of the individual, and genetic pedigree information. Optionally, a processor is integrated in the card member. The processor is operative to limit access to at least a portion of the information stored in the personal genome card (10).

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

|    |                          |    |                                       |    |                          |
|----|--------------------------|----|---------------------------------------|----|--------------------------|
| AM | Armenia                  | GB | United Kingdom                        | MW | Malawi                   |
| AT | Austria                  | GE | Georgia                               | MX | Mexico                   |
| AU | Australia                | GN | Guinea                                | NE | Niger                    |
| BB | Barbados                 | GR | Greece                                | NL | Netherlands              |
| BE | Belgium                  | HU | Hungary                               | NO | Norway                   |
| BF | Burkina Faso             | IE | Ireland                               | NZ | New Zealand              |
| BG | Bulgaria                 | IT | Italy                                 | PL | Poland                   |
| BJ | Benin                    | JP | Japan                                 | PT | Portugal                 |
| BR | Brazil                   | KE | Kenya                                 | RO | Romania                  |
| BY | Belarus                  | KG | Kyrgyzstan                            | RU | Russian Federation       |
| CA | Canada                   | KP | Democratic People's Republic of Korea | SD | Sudan                    |
| CF | Central African Republic | KR | Republic of Korea                     | SE | Sweden                   |
| CG | Congo                    | KZ | Kazakhstan                            | SG | Singapore                |
| CH | Switzerland              | LI | Liechtenstein                         | SI | Slovenia                 |
| CI | Côte d'Ivoire            | LK | Sri Lanka                             | SK | Slovakia                 |
| CM | Cameroon                 | LR | Liberia                               | SN | Senegal                  |
| CN | China                    | LT | Lithuania                             | SZ | Swaziland                |
| CS | Czechoslovakia           | LU | Luxembourg                            | TD | Chad                     |
| CZ | Czech Republic           | LV | Latvia                                | TG | Togo                     |
| DE | Germany                  | MC | Monaco                                | TJ | Tajikistan               |
| DK | Denmark                  | MD | Republic of Moldova                   | TT | Trinidad and Tobago      |
| EE | Estonia                  | MG | Madagascar                            | UA | Ukraine                  |
| ES | Spain                    | ML | Mali                                  | UG | Uganda                   |
| FI | Finland                  | MN | Mongolia                              | US | United States of America |
| FR | France                   | MR | Mauritania                            | UZ | Uzbekistan               |
| GA | Gabon                    |    |                                       | VN | Viet Nam                 |

5

10

PERSONAL HUMAN GENOME CARD AND METHODS  
AND SYSTEMS FOR PRODUCING SAME

15

Field of the Invention

The present invention relates to personal medical information cards.

20

Background of the Invention

The set of instructions for making an organism is called its genome. The genome for a human consists of coiled threads of deoxyribonucleic acid (DNA) and associated protein molecules found in every cell nucleus of the human. The components of these threads of DNA encode all of the information needed for building and maintaining life in the human.

Each DNA molecule contains a number of genes, which are the basic physical and functional units of heredity. A gene is a specific sequence of nucleotide bases within the human genome. The human genome is estimated to comprise approximately 50,000 to 100,000 genes. A number of these genes, estimated at 4000, are involved in an individual's predisposition to disease. The Human

Genome Project was initiated in 1990 with a goal of characterizing the entire human genome in order to devise improved strategies for disease identification, treatment, and prevention.

5           The prospect of determining an individual's predisposition to disease based on his/her genome has led some to warn of the potential for genetic-based discrimination in health insurance coverage. Here, genetic information could be used to exclude high-risk  
10 individuals from health care by either denying coverage or by charging prohibitive rates. The fear of discrimination may act to inhibit an individual from divulging his/her genetic status, even in light of the benefits of preventative measures and treatments which  
15 can be prescribed based on an early diagnosis of genetic predisposition to disease.

#### Brief Description of the Drawings

20           The invention is pointed out with particularity in the appended claims. However, other features of the invention will become more apparent and the invention will be best understood by referring to the following detailed description in conjunction with the  
25 accompanying drawings in which:

FIG. 1 is a block diagram of a system for producing a personal genome card in accordance with the present invention;

30           FIG. 2 is a flow chart of an embodiment of a method of producing a personal genome card for an individual;

FIG. 3 is a block diagram illustrating a system for storing information in a personal genome card;

FIG. 4 is an illustration of a PCMCIA embodiment of a personal genome card;

FIG. 5 is a block diagram of a smart card embodiment of a personal genome card; and

FIG. 6 is a block diagram illustrating a system for accessing a personal genome card.

5

#### Detailed Description of a Preferred Embodiment

Embodiments of the present invention advantageously provide a personal genome card containing a stored  
10 representation of an individual's genome. The personal genome card is sized to be carried by the individual for use in both medical and personal identification applications. Embodiments of the personal genome card limit external access to at least a portion of the  
15 representation of the individual's genome in order to avoid instances of genetic-based discrimination.

FIG. 1 is a block diagram of a system for producing a personal genome card 10 in accordance with the present invention. The personal genome card 10 includes a card  
20 member 12 which, preferably, is sized for carrying on an individual 14. For example, the card member 12 can be the size of a credit card for carrying within a wallet, a purse, or a pocket of the individual 14.

A machine-readable storage medium 16 is integrated  
25 in the card member 12. The machine-readable storage medium 16 is utilized to store personal genome information for the individual 14. The machine-readable storage medium 16 can be in the form of an electronic memory device, a magnetic memory device, or an optical  
30 memory device, for example. Preferably, the machine-readable storage medium 16 is non-volatile so that a powering signal need not be applied to maintain the personal genome information therein. Further, it is preferred that the machine-readable storage medium 16 be

rewriteable so that the information contained therein can be updated.

Also integrated within the card member 12 is an interface 18. The interface 18 is utilized to  
5 communicate the personal genome information between the machine-readable storage medium 16 and an exterior read/write device such as a computer.

A genetic screening apparatus 20 is utilized to screen at least a portion of a personal human genome 22  
10 of the individual 14. The genetic screening apparatus 20 forms the personal genome information to be stored in the personal genome card 10. The personal genome information is communicated to a data storing device 24 which performs a step of storing a representation  
15 thereof in the machine-readable storage medium 16. The data storing device 24 can be embodied a computer, for example, which communicates the personal genome information to the machine-readable storage medium 16 via the interface 18. In one embodiment, the personal  
20 genome card 10 includes a PC card, such as a PCMCIA card, having an internal memory for storing the personal genome information. Here, the interface 18 includes a PC card interface which is received by a mating PC card interface in the computer.

25 The personal genome information produced by the genetic screening apparatus 20 can be in any of a variety of forms. In one form, the genetic screening apparatus 20 determines a sequence of nucleotide bases for at least a portion of the personal human genome 22  
30 of the individual 14. The sequence of nucleotide bases can be determined from either a DNA sample or an RNA sample of the individual 14. The DNA or RNA sample can be sequenced to determine either a partial nucleotide

sequence or an entire nucleotide sequence of the personal human genome 22 of the individual 14.

Further, a sequence of nucleotide bases can be determined from a messenger RNA (mRNA) sample from the individual 14, or equivalently from copy DNA (cDNA) synthesized from the mRNA sample. The sequence of nucleotide bases in mRNA or cDNA is indicative of a protein-coding portion of the DNA, i.e. a gene of the individual 14. The existence of mRNA provides evidence of an active or expressed gene within the individual 14.

In these embodiments, the data storing device 24 stores a representation of the sequence of nucleotide bases, determined from any of the above-described approaches, in the machine-readable storage medium 16. For a DNA sample, the nucleotide bases within the sequence are selected from adenine (A), cytosine (C), guanine (G), and thymine (T). For an RNA sample, the nucleotide bases within the sequence are selected from adenine (A), cytosine (C), guanine (G), and uracil (U). Regardless of whether a DNA or an RNA sample is sequenced, the representation can include an uncompressed sequence of two-bit codes, wherein each two-bit code indicates one of four different nucleotide bases which comprise the sequence. Alternatively, the representation can include a lossless, compressed representation of the sequence. Various lossless data compression techniques can be utilized for this purpose.

Another form of personal genome information which can be determined by the genetic screening apparatus 20 is a genetic map for the individual 14. The genetic map is representative of positions of predetermined molecular markers within the DNA or RNA of the individual 14. The molecular markers can be determined using a restriction enzyme which cuts the DNA or the RNA

into fragments about a predetermined nucleotide subsequence. For example, a restriction enzyme can be utilized to determine the position of a molecular marker in the form of a G-A-T-C subsequence.

5       Using this form of personal genome information, the data storing device 24 stores a representation of the genetic map in the machine-readable storage medium 16. The representation can include a sequence of codes representative of distances between adjacent molecular  
10 markers. Alternatively, the representation can include a sequence of codes representative of absolute positions of the molecular markers. A lossless data compression technique can be utilized to produce a lossless, compressed representation based on either approach for  
15 storing the genetic map.

Regardless of its form, the personal genome information stored in the machine-readable storage medium 16 either directly or indirectly indicates if the individual 14 has a genetically-inherited disease and/or  
20 a genetic predisposition to a disease. If so, an appropriate treatment strategy can be formulated by medical personnel.

The foregoing description of preferred embodiments of the present invention is based on a nucleotide  
25 sequence form for the personal genome information. It is noted, however, that alternative embodiments may utilize other forms for the personal genome information, such as a genetic map form.

FIG. 2 is a flow chart of an embodiment of a method  
30 of producing a personal genome card for an individual. The method includes a step of providing the card member 12 having the machine-readable storage medium 16 integrated therein, as indicated by block 40. A smart



card or a PC card, such as a PCMCIA card, can be utilized to provide the card member 12.

As indicated by block 42, a step of determining a first sequence of nucleotide bases for at least a portion of a genome of the individual 14 is performed. The first sequence of nucleotide bases can be determined by a genetic sequencing apparatus in the genetic screening apparatus 20. If desired, the sequence of nucleotide bases can be determined for an entire exon, for an entire gene, for an entire chromosome, or for the entire genome of the individual 14.

A step of storing a representation of the first sequence in the machine-readable storage medium 16 is performed, as indicated by block 44. The step of storing the representation of the first sequence can include compressing the first sequence to form lossless, compressed data, and storing the lossless, compressed data in the machine-readable storage medium. If the first sequence includes an exon or a gene having a predetermined sequence, the lossless, compressed data can include a code which identifies the predetermined sequence for the exon or the gene. For example, if the exon or the gene has a sequence observed in other individuals, a single code can be utilized to compress the representation of the sequence.

Alternatively, if the first sequence includes an exon or a gene which is either a corrupted or a mutated version of a predetermined sequence, the lossless, compressed data can include a first code identifying the predetermined sequence and a second code indicating the corruption or the mutation. The corruption or the mutation can be present at the birth of the individual 14 or can be incident-based, i.e. an aberration from the individual's genes at birth.

As indicated by block 46, the method can include a step of storing, in the machine-readable storage medium 16, phenotype information for the individual 14. Preferably, the phenotype information is associated with genotype information encoded by the first sequence. The method can further include a step of storing, in the machine-readable storage medium 16, a personal medical history for the individual 14, as indicated by block 48.

Optionally, the method can include steps of storing genome information and medical information for one or more family members of the individual 14. In particular, a step of determining a second sequence of nucleotide bases for at least a portion of a genome of a family member of the individual 14 is performed, as indicated by block 50. A step of storing a representation of the second sequence of nucleotide bases in the machine-readable storage medium 16 is performed, as indicated by block 52. As indicated by block 54, a step of storing, in the machine-readable storage medium 16, phenotype information for the family member is performed. Further, a step of storing a personal medical history for the family member can be performed as indicated by block 56.

The steps indicated by blocks 50, 52, 54, and 56 can be repeated for a plurality of family members of the individual 14. Preferably, the plurality of family members include at least one ancestor of the individual 14, such as a mother and/or a father of the individual 14. By including genotype information and medical history for at least one ancestor of the individual 14, the personal genome card 10 contains genetic pedigree information for the individual 14. The genetic pedigree information is useful for predicting diseases whose onset are probabilistic for individuals having a

predetermined disease gene. For example, if a disease gene is identified in the genome of the individual 14, the genetic pedigree information can be referred to determine if ancestors of the individual 14 having the same disease gene expressed a corresponding disease.

FIG. 3 is a block diagram illustrating a system for storing information in a personal genome card 60. A computer 62 or like programmable apparatus receives or determines a first sequence of nucleotide bases 64 for the individual 14, phenotype information 66 for the individual 14, a personal medical history 68 for the individual 14, a second sequence of nucleotide bases 70 for at least one family member of the individual 14, phenotype information 72 for the family member, a personal medical history 74 for the family member, and identification information 76 (such as name, social security number, or insurance number) for the individual 14. The computer 62 stores this information in a storage medium 78 interfaced to the computer 62 via an interface 80. The system described is amenable to a PCMCIA embodiment of the personal genome card 60, wherein the interface 80 is a PCMCIA interface.

FIG. 4 is an illustration of a PCMCIA embodiment of a personal genome card 90. The personal genome card 90 includes a card member 92 having a PCMCIA interface 94. A storage medium (not illustrated) such as a memory is integrated within the card member 92. Here, the personal genome card 90 can be received in a PCMCIA port on the computer 62 for storing personal genome information, personal medical history, and pedigree information in the memory.

FIG. 5 is a block diagram of a smart card embodiment of a personal genome card 100. Similar to the embodiment of FIG. 1, the personal genome card 100

includes a machine-readable storage medium 102 and an interface 104 integrated within a card member 106.

In addition, a processor 108 is integrated in the card member 106. The processor 108 is operative to  
5 limit external access to predetermined information stored in the machine-readable storage medium 102. The access is allowed or denied based upon whether a predetermined access code is provided to the processor 108. The predetermined access code can be a secret code  
10 known only by the individual 14. The processor 108 receives the predetermined access code via the interface 104 or via a user interface 109 incorporated in the card member 106. Having the user interface 109 (such as a series of buttons) incorporated in the card member 106  
15 allows the individual 14 to enter the predetermined access code without having to divulge the predetermined access code to others.

Preferably, the processor 108 does not limit external access to personal medical information which  
20 would be vital in an emergency medical situation where communication with the individual 14 is either impaired or impossible. However, the processor 108 does limit external access to at least a portion of the personal genome information. This access is limited to avoid a  
25 possibility of discrimination in obtaining health insurance or discrimination in hiring based on having a genetic predisposition to a disease.

The processor 108 can also be operative to decompress the lossless, compressed data stored on the  
30 machine-readable storage medium 102. As a result, decompressed data is communicated via the interface 104.

To produce the smart card embodiment of the personal genome card, a step of integrating the processor 108 in the card member 106 is performed in

addition to the steps illustrated in FIG. 2. This step can include storing the predetermined access code and access software either in the processor 108 or the machine-readable storage medium 102.

5        FIG. 6 is a block diagram illustrating a system for accessing a personal genome card 110. The personal genome card 110 communicates with an on-line system 112. The on-line system 112 accesses the information stored  
10        in a machine-readable storage medium 111 for analysis and/or display. The on-line system 112 can be located remotely from the personal genome card 110, as illustrated in FIG. 6, or can be co-located with the personal genome card 110.

      The personal genome card 110 is received by an  
15        interface 114. The interface 114 mates with an interface 116 within the personal genome card 110. For remote access, a modem 118 is coupled to the interface 114 to communicate data with a remote modem 120. The modem 118 can communicate with the remote modem 120  
20        using either a wireline link or a wireless link. The remote modem 120 communicates the data to a computer system having a computer 122, a user interface 124 (e.g. a keyboard and/or a mouse), and a display device 126 (e.g. a computer monitor). If the personal genome card  
25        110 is co-located with the on-line system 112, the modem 118 and the remote modem 120 are not required.

      The on-line system 112 can be utilized by medical personnel to diagnose the individual's genetic condition. The medical personnel can navigate the  
30        information stored the personal genome card 110 by entering navigation instructions into the user interface 124. The navigation instructions are communicated to the personal genome card 110 by the remote modem 120, the modem 118, and the interface 114. In response

thereto, the personal genome card 110 communicates either compressed data or uncompressed data to the computer 122 by the interface 114, the modem 118, and the remote modem 120. If compressed data is  
5 transmitted, the computer 122 includes decompression software to decompress the personal genome information. As an alternative to remotely controlling which of the personal genome information is transmitted, a predetermined amount of the data can be transmitted to  
10 the computer 122.

The computer 122 is utilized for analysis and/or display of the personal genome information, the personal medical history, and the pedigree information. Medical personnel can use the analysis of the personal genome  
15 information to determine if the individual 14 has a genetically-inherited disease or a genetic predisposition to a disease. Further, a doctor can compare the personal genome information in the personal genome card 110 to more-recently screened information to  
20 determine if any mutations have occurred since a previous screening. The personal medical history can be utilized to determine if the individual 14 has previously exhibited any symptoms of the disease. The pedigree information can be utilized to gauge the  
25 likelihood of an onset of the disease based on the genome and medical history of the individual's ancestors. The personal genome information is also useful in prescribing drugs which will not adversely affect the individual 14.

30 The on-line system 112 can also be utilized for remote identification purposes. Here, the on-line system 112 contains a database 130 of personal genome information for a plurality of individuals, and compares the personal genome information received from the

personal genome card 110 thereto. The on-line system 112 can also be utilized to store updates of an individual's genome over his/her lifetime.

Thus, there has been described herein a concept, as  
5 well as several embodiments including preferred  
embodiments of a personal human genome card and a method  
and system of producing the same.

Because the various embodiments of the present  
invention store personal genome information in a card  
10 which can be carried by an individual, they provide a  
significant improvement in that the card can be used by  
medical personnel to determine if the individual has a  
genetic predisposition to disease. As more disease  
genes are identified in scientific research, the  
15 personal genome information in the personal genome card  
can be reviewed as a preventative diagnostic procedure.  
As a result of the preventative diagnostic, medical  
personnel may prescribe preventative measures for the  
individual to reduce a likelihood of acquiring a  
20 disease.

Additionally, the various embodiments of the  
present invention as herein-described limit external  
access to at least a portion of the personal genome  
information in order to avoid genetic-based  
25 discrimination.

It will be apparent to those skilled in the art  
that the disclosed invention may be modified in numerous  
ways and may assume many embodiments other than the  
preferred form specifically set out and described above.

30 Accordingly, it is intended by the appended claims  
to cover all modifications of the invention which fall  
within the true spirit and scope of the invention.

What is claimed is:

## Claims

1. A method of producing a personal genome card for an individual, the method comprising the steps of:
- 5 providing a card member having a machine-readable storage medium integrated therein, the card member sized for carrying on the individual;
- determining a first sequence of nucleotide bases for at least a portion of a genome of the individual;
- 10 and
- storing a representation of the first sequence in the machine-readable storage medium.
2. The method of claim 1 wherein the step of
- 15 storing the representation of the first sequence includes:
- compressing the first sequence to form lossless, compressed data; and
- storing the lossless, compressed data in the
- 20 machine-readable storage medium.
3. The method of claim 1 further comprising the step of storing phenotype information for the individual on the machine-readable storage medium.
- 25
4. The method of claim 1 further comprising the steps of:
- determining a second sequence of nucleotide bases for at least a portion of a genome of an ancestor of the
- 30 individual; and
- storing a representation of the second sequence in the machine-readable storage medium.



5. A personal genome card for an individual, the personal genome card comprising:

a card member sized for carrying on the individual;

a machine-readable storage medium integrated in the

5 card member; and

machine-readable data stored on the machine-readable storage medium, the machine-readable data including a representation of a first sequence of nucleotide bases for at least a portion of a genome of  
10 the individual.

6. The personal genome card of claim 5 wherein the first sequence includes an entire nucleotide sequence of the genome of the individual.

15

7. The personal genome card of claim 5 wherein the representation includes lossless, compressed data for the first sequence.

20

8. The personal genome card of claim 7 wherein the first sequence includes a gene having a predetermined sequence, and wherein the lossless, compressed data includes a code which identifies the predetermined sequence for the gene.

25

9. The personal genome card of claim 5 wherein the machine-readable data further includes phenotype information for the individual.

30

10. The personal genome card of claim 5 wherein the machine-readable data further includes a representation of a second sequence of nucleotide bases for at least a portion of a genome of an ancestor of the individual.

2/3

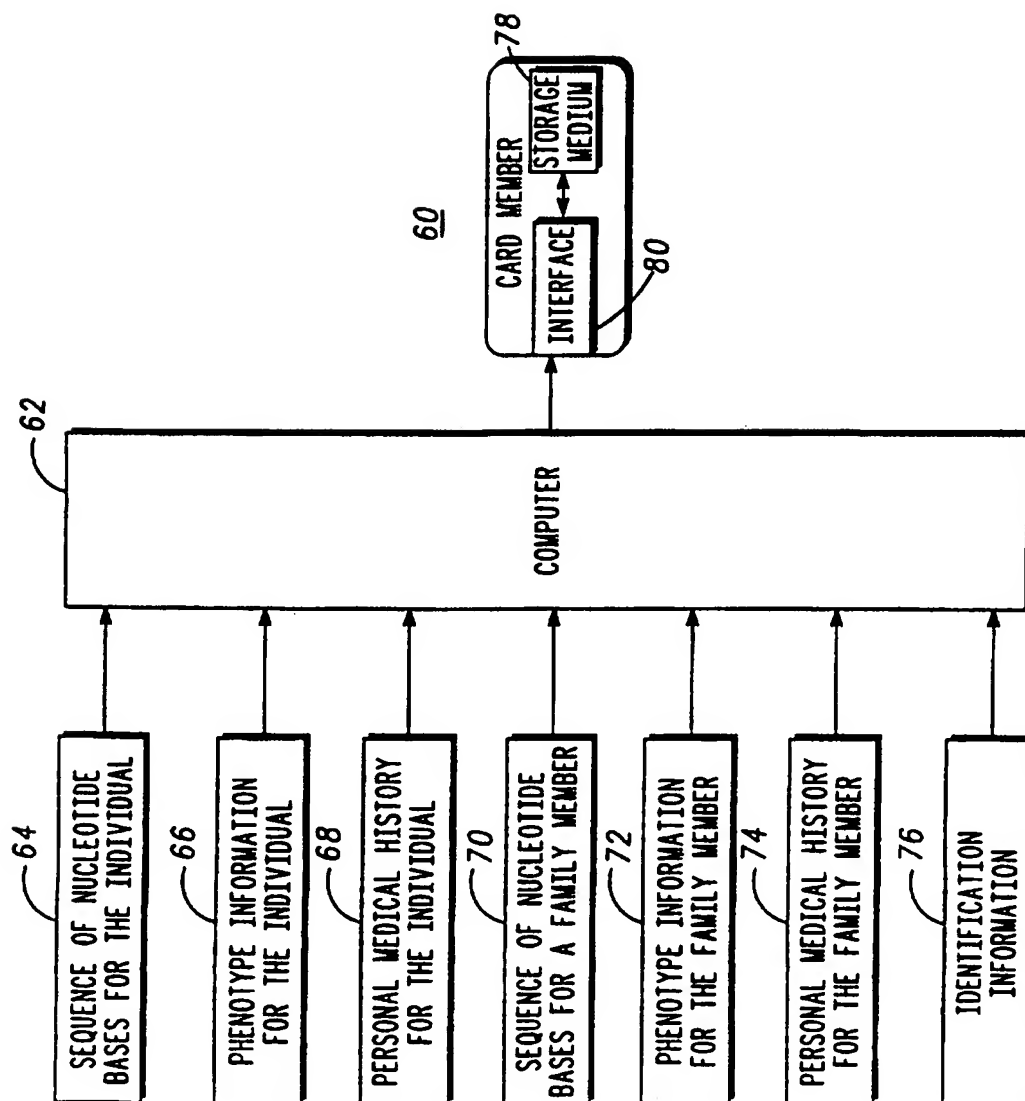


FIG. 3

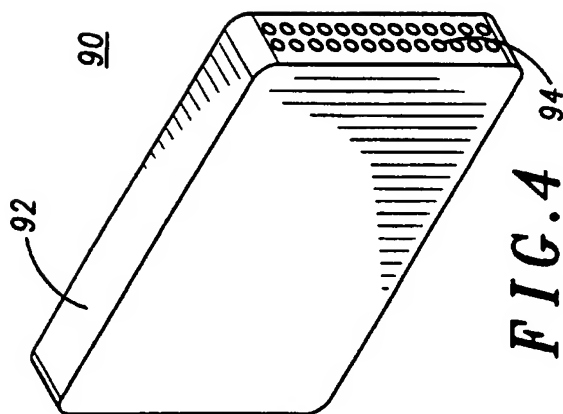
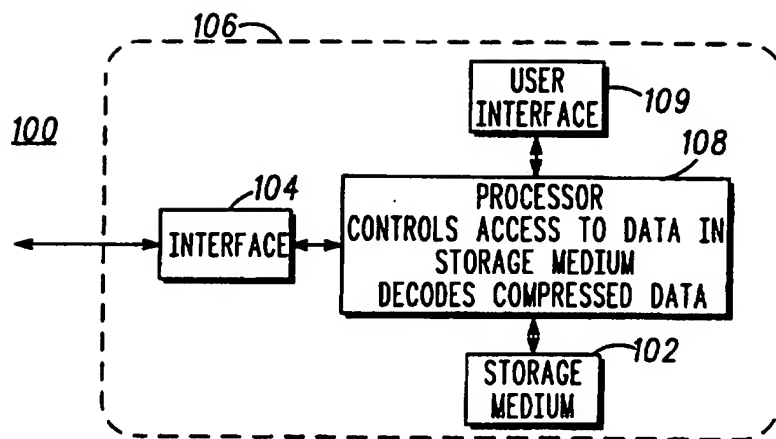
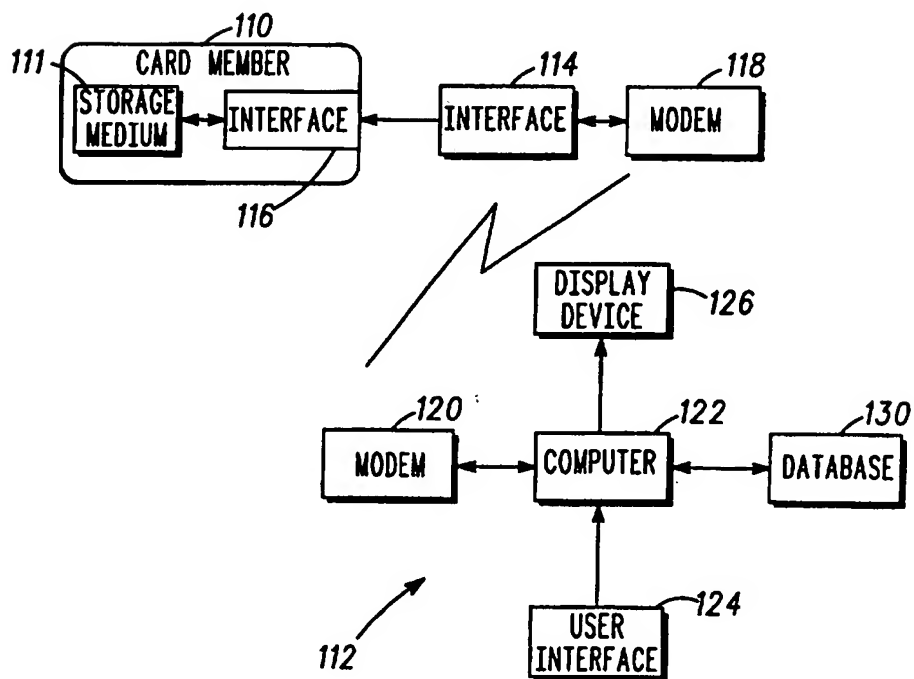


FIG. 4

3/3

**FIG. 5****FIG. 6**

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US96/19690

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : G06K 7/08

US CL : 364/496; 235/492;

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 364/413.01, 413.02, 496-498; 235/492

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
APS, DIALOG

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| Y         | US 5,473,690 (GRIMONPREZ et al) 05 December 1995, col. 1, lines 7-23.              | 1-10.                 |
| Y         | US 5,196,682 (ENGLEHARDT) 23 March 1993, col. 8, lines 33-43.                      | 1-10.                 |
| Y         | US 4,891,506 (YOSHIMATSU) 02 January 1990, col. 3, line 62- col. 4, line 14.       | 1-10.                 |
| Y         | US 5,371,671 (ANDERSEN et al) 06 December 1994, col. 2, lines 2-15, 36-42.         | 1-10.                 |
| Y         | US 4,982,326 (KANEKO) 01 January 1991, col. 13, lines 50-56.                       | 1-10.                 |
| Y         | US 4,802,101 (HARA) 31 January 1989, col. 8, lines 8-26.                           | 1-10.                 |

☒ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

|   |  |
|---|--|
| * Special categories of cited documents:  | *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| *A* document defining the general state of the art which is not considered to be part of particular relevance   | *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| *E* earlier document published on or after the international filing date  | *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | *A* document member of the same patent family  |
| *O* document referring to an oral disclosure, use, exhibition or other means  |  |
| *P* document published prior to the international filing date but later than the priority date claimed  |  |

Date of the actual completion of the international search

20 MARCH 1997

Date of mailing of the international search report

15 APR 1997

 Name and mailing address of the ISA/US  
 Commissioner of Patents and Trademarks  
 Box PCT  
 Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

EMANUEL T. VOELTZ

Telephone No. (703) 305-9714

**INTERNATIONAL SEARCH REPORT**International application No.  
PCT/US96/19690**C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| A         | US 5,291,399 (CHACO) 01 March 1994.  | 1-10.                 |
| A         | US 4,852,570 (LEVINE) 01 August 1989.  | 1-10.                 |